

## REMARKS

Claims 36, and 43-50 are pending. Claim 36 is currently amended. Claims 1-35 and 37-42 are canceled. No new matter is added. Applicants respectfully request reconsideration of the rejections.

The rejection of claims 33 and 38-42 under 35 U.S.C. 102(a) is made moot by cancellation of the claims.

Claims 36 and 43-50 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Hallenbeck *et al.* (WO96/17053) in view of Richards *et al.* (WO 95/14100). Applicants respectfully submit that the presently claimed invention is not made obvious by the cited combination of art.

The disclosure in Hallenbeck (WO 96/17053) includes a description of adenoviral vectors that contain a gene which is essential for replication, operably linked to a heterologous transcriptional regulatory sequence, such that replication is conditioned on the presence of a trans-acting transcriptional regulatory factor. The publication describes the adenovirus E1a or E1b gene may be operably linked to a tissue-specific transcriptional regulatory sequence and a vector which encodes a heterologous gene product that is toxic for the target tissue.

While Hallenbeck *et al* recite a variety of transcriptional regulatory sequences (with examples recited, including: carcinoembryonic antigen (CEA), DE3, alpha-fetoprotein (AFP), Erb-B2, surfactant, especially lung surfactant, and the tyrosinase promoter), there is no teaching or suggestion that greater specificity or unexpected benefits could be obtained from the use of two different TREs to regulate a first and second adenovirus gene.

The additional TRE and the heterologous feature, which features are recited in all of the claims of the present application, add unexpected advantages to the virus. The Patent Office has previously acknowledged in commonly owned patents, *e.g.* U.S. Patent no. 6,585,968; and U.S. Patent no. 6,436,394 that the prior art does not teach two different TREs in such an adenoviral vector.

Applicants further submit that the specific CEA enhancer sequence set forth in the present claims could not have been predicted from the cited art. A copy of a Declaration made under 37 C.F.R. 1.132 by Dr. De-Chao Yu, which was of record in the immediate parent to the present application, USSN 09/033,555, is provided herewith, which describes the unexpected benefits of the specific sequences in the CEA-TRE.

As described by Dr. Yu in paragraph 3 of the Declaration, the CEA promoter primers

described by Hallenbeck (page 41, table 1) would not isolate the CEA enhancer sequence utilized by Applicants. The CEA sequences in the presently claimed adenoviral vectors provide for significantly increased specificity compared to an adenovirus vector comprising the sequences obtained by the methods of Hallenbeck. Hence, Hallenbeck teaches away from the claimed TRE sequences.

Because Hallenbeck leads the practitioner to utilize a different CEA regulatory sequence, Hallenbeck does not provide one of skill in the art with guidance useful to isolate the claimed enhancer sequences from the sequence taught by Richards *et al.*

As previously argued, Richards *et al.* (WO95/14100) is directed to transcriptional regulatory sequences (TRSs) for use in targeted gene therapy, where a tumor specific TRS is used to regulate the expression of a heterologous enzyme, typically a non-mammalian enzyme, that is cytotoxic to tumor cells, i.e. cytosine deaminase together with 5-FC (page 5, lines 7-19; page 8, lines 9-14 and page 15, line 31- page 17, line 15). More specifically, Richards *et al.* describe the use of a CEA-TRS and its effect in regulating expression of reporter constructs, exemplified by use of a retroviral shuttle vector containing a luciferase reporter gene. Richards *et al.* do not describe or suggest the replication competent adenoviral vectors for selective cytolysis of a target cell encompassed by the present claims.

More importantly, if one reviews the data shown in Figure 5D of Richards *et al.*, which is the figure relevant for selectivity, it is seen that even in the best construct/cell combinations (pCR136; pCR137 in LoVo cells), no better than about a 35% increase is with respect to expression in non-permissive Hep3B cells, and in most cases is a more modest increase of 10 to 20%. This is quite different from the selectivity shown in the context of replication competent adenoviral vectors, as indicated in Paragraph 5 of the declaration of Dr. Yu, wherein the vectors that had a TRE which included a CEA promoter and enhancer had a selectivity for CEA-expressing cells of from 150 to 1000 fold.

The constructs claimed by Applicants provide for a level of selectivity that could not have been predicted from the teachings of the prior art, by utilizing a particularly desirable CEA enhancer/promoter combination. One of skill in the art would not have had a reasonable expectation of success without the teachings of the present invention.

In view of the above remarks, Applicants respectfully submit that the presently claimed invention is not anticipated or made obvious by the cited references. Withdrawal of the rejections is requested.

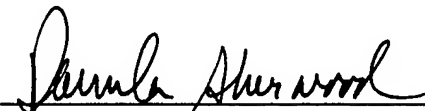
CONCLUSION

Applicants submit that all of the claims are now in condition for allowance, which action is requested. If the Examiner finds that a Telephone Conference would expedite the prosecution of this application, she is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any other fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815, order number CELL-007CON.

Respectfully submitted,

Date: August 4, 2004

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PATENT  
Docket No. 348022000500

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Henry LAMPARSKI et al.

Serial No.: 09/033,555

Filing Date: March 2, 1998

For: ADENOVIRUS VECTORS SPECIFIC  
FOR CELLS EXPRESSING  
CARCINOEMBRYONIC ANTIGEN  
AND METHODS OF USE THEREOF

Examiner: R. Schwartzman

Group Art Unit: 1636

**DECLARATION OF DE-CHAO YU  
PURSUANT TO 37 C.F.R. § 1.132**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

I, De-Chao Yu, declare as follows:

1. I am currently Vice President of Research at Calydon Inc., Assignee of the above-identified patent application. My Curriculum Vitae is attached as Exhibit 1.
2. I am an expert in the field of DNA cloning and adenovirus technology. I have read the above-identified application and have reviewed the pending claims. I have also read the Office Action dated July 26, 2000.
3. I have reviewed the Hallenbeck et al. PCT publication PCT/US95/15455 ("the Hallenbeck publication"). The carcinoembryonic antigen (CEA) promoter oligonucleotide primers disclosed at page 41, Table 1, that is: 5' GAC CCG GGC GCG CCT CTG TCA CCT TCC TGT TGG 3' and  
5' CGA GAT CTA CTA GTT CTC TGC TGT CTG CTC TGT C 3'

would isolate a CEA DNA fragment from nucleotide -362 to +105 relative to the transcription start site for the CEA gene. A schematic illustration showing the primer alignment within the region of the CEA TRE disclosed in Figure 2 of the above-identified application is attached as Exhibit 2. This nucleotide region of CEA which would be isolated by the primers disclosed in the Hallenbeck publication does not contain any nucleotide sequence from about -14.5 to about -3.8 relative to the transcriptional start site of the CEA gene as shown in Figure 2. Replication-competent adenovirus containing a CEA enhancer nucleotide sequence within the region from about -14.5 to about -3.8 relative to the transcriptional start site of the CEA gene shows significantly increased specificity as compared to a replication-competent adenovirus containing a CEA promoter nucleotide sequence within about -402 to about +69 relative to the transcriptional start site of the CEA gene and lacking a CEA enhancer nucleotide sequence within the region from about -14.5 to about -3.8 relative to the transcriptional start site of the CEA gene.

4. To compare the effect of a CEA enhancer nucleotide sequence within the region from about -14.5 to about -3.8 relative to the transcriptional start site of the CEA gene on virus replication, I constructed a replication-competent adenovirus vector containing the adenovirus gene E1A under the control of a CEA-TRE that contained (a) a CEA promoter containing a nucleotide sequence from about -402 to about +69 relative to the transcriptional start site, that is from nucleotide -301 to nucleotide +69 of the nucleotide sequence as shown in Figure 2; and (b) an enhancer nucleotide sequence within the region from about -14.5 to about -3.8 with respect to the transcriptional start site, that is from nucleotide -6072 to -3916 of the nucleotide sequence as shown in Figure 2. This adenovirus vector was used to create an adenovirus designated CV798. I also constructed a replication-competent adenovirus vector containing the adenovirus gene E1A under control of a CEA-TRE that contained a CEA promoter containing a nucleotide sequence from about -402 to about +69 relative to the transcriptional start site, that is from nucleotide -301 to nucleotide +69 of the nucleotide sequence as shown in Figure 2, and that does not contain any other CEA sequences, including the enhancer found within the nucleotide sequence from about -14.5 to about -3.8 relative to the transcriptional start. This adenovirus vector was used to create an adenovirus designated CV799.

5. CV798, CV799 and a control, wild-type adenovirus, designated as CV802, were used to infect CEA producing cell lines LoVo, SW1463 and NCI-H508 and CEA non-producing cell lines, U118MG, PA-1 and G361. Adenovirus replication was measured by virus plaque

efficiency as described in the above-identified application, in particular under Example 2 at page 58. Virus replication for CV798 and CV799 was normalized against virus replication for the control, CV802. The results are shown in Table 1 which provides normalized virus replication efficiency of CV798 and CV799 as measured by plaque formation per cell, that is, pfu/cell.

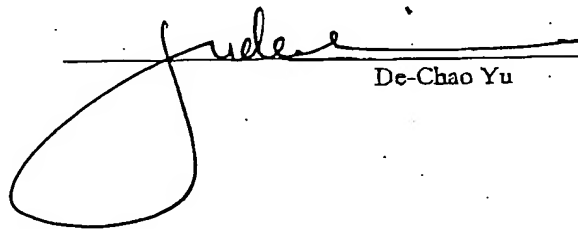
**Table 1: Normalized virus replication efficiency (pfu/cell)**

Cell Line	CV802 control	CV798 promoter and enhancer	CV799 promoter only	CV798/CV802	CV799/CV802
LoVo (CEA+)	1.0	0.52	0.49	0.52	0.49
SW1463 (CEA+)	1.0	0.47	0.48	0.47	0.48
NCI-H508 (CEA+)	1.0	0.45	0.34	0.45	0.34
U118MG (CEA-)	1.0	0.00033	0.25	0.00033	0.25
PA-1 (CEA-)	1.0	0.0001	0.18	0.0001	0.18
G361 (CEA-)	1.0	0.003	0.17	0.003	0.17

6. The results show that CV798 preferentially replicates in and destroys CEA-producing cells, with a cytolytic selectivity of CEA-producing cells vs. non-CEA producing cells of as much as about 1000:1 and at least about 150:1. The results show that CV799 preferentially replicates in and destroys CEA-producing cells, with a cytolytic selectivity of CEA-producing cells vs. non-CEA producing cells of about 3:1 or at least about 2:1. The presence of a CEA enhancer nucleotide sequence within the region from about -14.5 to about -3.8 relative to the transcription start site of the CEA gene in a replication-competent adenovirus significantly increases cytolytic selectivity of the adenovirus for CEA-producing cells. The data also show a decrease in viral replication in CEA non-producing cells with CV798.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

2/9/2001  
Date

  
De-Chao Yu

**DECHAO 'DC' YU**

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EMAIL: [dyu@calydon.com](mailto:dyu@calydon.com)**PROFESSIONAL EXPERIENCE****Vice President of Research and Development****Calydon, Inc., Sunnyvale, CA ([www.calydon.com](http://www.calydon.com))****1999-to-date**

As an officer of the Company, I have been responsible for the Discovery research, Preclinical Pharmacology/Toxicology, Product Development and Manufacturing with a staff of 23 including 8 Ph.D./MD scientists. Created and developed 5 anti-cancer product leads two of which are currently in clinical development. Coordinated with our collaborators or contractors in preclinical pharmacology and toxicology studies. Managed product manufacturing for Phase I and II clinical trials.

**Director of Research****Calydon, Inc., Sunnyvale, CA****1997-99****Group Leader of Research****Calydon, Inc., Sunnyvale, CA****1996-97****Assistant Research Molecular Virologist****Department of Pharmaceutical Chemistry, University of California-San Francisco, San Francisco, CA****1995-96**

An investigator of a NIH grant-funded research on the characterization of Giardavirus (GLV) gene expression and the development of a virus-mediated gene transfection system for an ancient eukaryote *Giardia lamblia*. Resulted in 7 peer-reviewed first author publications.

- Identified replicational and transcriptional regulatory elements as well as viral RNA packaging signal in the GLV dsRNA genome. (Mol. Biochem. Parasitology 110:417, 2000)
- Created an infectious virus-like particle for potential treatment of giardiasis. (J. Virology 70:8752, 1996)

**Post-Doctoral Fellow****University of California-San Francisco, San Francisco, CA****1993-95**

- Developed the first gene transfection system for the most ancient eukaryote: *Giardia lamblia*. (Mol. Cell. Biology 15:4867, 1995; Mol. Biochem. Parasitology 83:81, 1996)
- Discovered the coding sequence of the GLV capsid protein that is attributed to enhanced translation efficiency in the most ancient eukaryote *G. lamblia*. (Mol. Biochem. Parasitology 96: 151, 1998)
- Discovered a virus-induced host cysteine protease involved in the maturation of the GLV capsid protein. (J. Virology 69: 2825, 1995)
- Cloned and determined the terminal sequences of the GLV double-stranded RNA genome. (RNA 2:824, 1996)

**Ph.D. student/Research Associate****Chinese Academy of Sciences, Shanghai, P. R. China****1989-93**

- Elucidated the mechanisms by which the TMV coat protein subgenomic RNA arises and generated a series of transgenic tobaccos to investigate how the TMV subgenomic promoter works in vivo. (Chinese J. Virology 12:254, 1996)
- Explored a new genetic engineering strategy for tobacco to create resistance against tobacco mosaic virus (TMV). (Chinese J. Virology 12:243, 1996)

**Research Associate****Nanjing Forestry University, Nanjing, P. R. China****1986-89**

Investigated the physiological and biochemical effects of plant growth regulators and hormones on plant growth.

**PATENTS**

Inventor of 12 issued and pending patents that cover tumor-specific genes, tumor-specific oncolytic viruses, a new function of the adenovirus E3 region, and a medical device, including:

1. US 6,051,417. Henderson DR, Lamparski H, Schuur E and Yu DC. Prostate cancer drug screening using hKLK2 enhancer. 4/18/2000.



2. WO 98/05797. Henderson D, Lamparski H, Schuur E, and Yu DC. *Prostate cancer drug screening.*
3. WO 98/39467, EP0968298. *Adenovirus vectors specific for cells expressing carcinoembryonic antigen and methods of use thereof.*
4. WO 98/39466. Yu DC, Schuur E, and Henderson D. 1998. *Adenovirus vectors specific for cells expressing androgen receptor and methods of use thereof.*
5. WO 98/39464. Yu DC, and Henderson D. 1998. *Adenovirus vectors containing heterologous transcription regulatory elements and methods of use thereof.*
6. WO 99/06576. Yu DC, Henderson D, and Schuur E. 1999. *A human glandular kallikrein enhancer, vectors comprising the enhancer and methods of use thereof.*
7. WO 00/15820. Yu DC and Henderson DR. 2000. *Adenovirus vectors containing cell status-specific response elements and methods of use thereof.*
8. WO 00/39317. Henderson DR and Yu DC. *Target cell-specific adenoviral vectors containing E3 and method of use thereof.*
9. WO 00/20041, AU 1109300. Yu DC, Henderson DR and Chen Y. *Methods of enhancing effectiveness of therapeutic viral immunogenic agent administration.*
10. Yu DC. *Cell specific adenovirus vectors comprising an internal ribosome entry site.* Filed March 2000.
11. Yu DC. *Methods of treating neoplasia with combining of target cell-specific adenovirus, chemotherapy and radiation.* Filed March 2000.
12. Yu DC. *Human urothelial cell specific uroplakin transcriptional regulatory sequences, vectors comprising an uroplakin transcriptional regulatory sequences, and methods of use thereof.* Filed March 2000.

#### PUBLICATIONS

1. Zhang H, Chen Y, Nguyen N, Henderson DR and Yu DC. 2001. Identification of human uroplakin II promoter and its use in the construction of an Adenovirus variant which specifically replicates in bladder transient cell carcinoma. (in preparation)
2. Li Y, Dilley J, Henderson D, and Yu DC. 2001. Interaction between E1B 19K protein and the immunomodulatory proteins in the Ad E3 region leads to a better cytotoxicity. (Submitted)
3. Chen Y, DeWeese T, Dilley J, Zhang Y, Nguyen N, Lee J, Li Y, Ramesh, Ilves H, Pennathur-Das R, Radzynski, Wypych J, Memarzadeh E, Karpf D, Henderson D, and Yu DC. 2001. Prostate cancer-specific Adenovirus variant in combination with irradiation produces synergistic antitumor efficacy without increase in toxicity. (Submitted)
4. Henderson DR, Li Y, Chen Y and Yu DC. 2001. CV890, a self-inactivating attenuated replicating adenovirus that preferentially replicates in AFP-producing human hepatocellular carcinoma cells (submitted)
5. DeWeese TL, van der Poel H, Li S, Mikhak B, Drew R, Goemann M, Hamper U, DeJong R, Detorie N, Rodriguez R, Haulk T, DeMarzo A, Piantadosi S, Chen Y, Yu DC, Henderson D, Karpf D, Sommer J, Carducci MA, Nelson WG, and Simons JW. 2001. A phase I trial of CV706, a replication competent, PSA selective oncolytic adenovirus, for the treatment of locally recurrent prostate cancer following radiation therapy. (submitted)
6. Yu DC, Chen Y, Dilley J, Li Y, Embry M, Zhang H, Nguyen N, Oh J, and Henderson DR. 2001. Antitumor synergy of CV787, a prostate-specific Adenovirus, and paclitaxel and docetaxel *Cancer Research* 61: 517-525.
7. Yu DC, Wang AL, and Wang CC. 2000. The putative transcription initiation site in Giardavirus double-stranded RNA genome. *Molecular and Biochemical Parasitology* 110: 417-421
8. Chen Yu, Yu DC, Charlton D. and Henderson DR. 2000. Pre-existent Adenovirus antibodies inhibit systemic toxicity and anti-tumor activity of CV706 in the nude mouse LNCaP xenograft model: implications and proposals for human therapy. *Human Gene Therapy* 11: 1553-1567

9. Yu DC, Chen Y, Seng M, Dilley J, and Henderson DR. 1999. The addition of Ad5 region E3 enables Calydon virus 787 to eliminate distant prostate tumor xenografts. (Published erratum of Figure 8C appears in *Cancer Research* 60(4): 1150, 2000).  
*Cancer Research* 59: 4200-4203
10. Yu DC, Sakamoto GT and Henderson DR. 1999. Identification of the transcriptional regulatory sequences of human kallikrein 2 and their use in the construction of Calydon virus 764, an attenuated replication competent adenovirus for prostate cancer therapy.  
*Cancer Research* 59:1498-1504
11. Yu DC, Wang AL, Botka CW, and Wang CC. 1998. Protein synthesis in *Giardia lamblia* may involve interaction between a downstream box (DB) in mRNA and an anti-DB in the 16S-like ribosomal RNA.  
*Molecular and Biochemical Parasitology* 96: 151-165.
12. Yu DC, Wang AL and Wang CC. 1996. Amplification, expression and packaging of a foreign gene by giardiavirus in *Giardia lamblia*.  
*Journal of Virology* 70:8752-8757
13. Yu DC, Liu NZ and Wang J. 1996. Further studies on the synthesis of tobacco mosaic virus coat protein subgenomic RNA in tobacco protoplasts.  
*Chinese Journal of Virology* 12:254-266
14. Wang J, Yu DC and Liu NZ. 1996. Positive-strand RNA produced from negative-strand RNA containing coat protein subgenomic promoter of tobacco mosaic virus.  
*Chinese Journal of Virology* 12:243-253
15. Yu DC and Wang CC. 1996. Identification of cis-acting signals in the giardiavirus (GLV) genome required for expression of firefly luciferase in *Giardia lamblia*.  
*RNA* 2:824-834.
16. Yu DC, Wang AL and Wang CC. 1996. Stable coexpression of a drug-resistance gene and a heterologous gene in an ancient parasitic protozoan *Giardia lamblia*.  
*Molecular and Biochemical Parasitology* 83:81-91.
17. Yu DC, Wang AL, Wu CH, and Wang CC. 1995. Virus-mediated expression of firefly luciferase in the parasitic protozoan *Giardia lamblia*.  
*Molecular and Cellular Biology* 15:4867-4872.
18. Yu DC, Wang CC, and Wang AL. 1995. Maturation of giardiavirus capsid protein involves in posttranslational proteolytic processing by a cysteine protease.  
*Journal of Virology* 69:2825-2830.
19. Yu DC. 1993. Regulation and expression of the subgenomic RNAs of plant positive-strand RNA viruses.  
*Ph.D. Dissertation, Chinese Academy of Sciences.*
20. Yu DC. 1993. Progress and assessment on the genetic engineering strategies for virus resistance in plants.  
*Plant Physiology Communications* 2:141-147
21. Yu DC and Wang J. 1992. Increase of the efficiency on production of the (+)-strand RNA from the (-)-strand RNA with TMV-CP SGP by a nonsensical RNA.  
*The Annual Report (1991/1992) of National Laboratory of Plant Molecular Genetics*, 2:15-16
22. Yu DC and Wang AL. 1990. The physiological effects of Triacantanol (TA) on *Pinus elliotii engelmannii* seedlings.  
*Journal of Nanjing Forestry University* 14:8-14.
23. Wang AL and Yu DC. 1990. Studies on controlling hair-like fiber pollution of *Platanus Hispanica Muechh.*  
*Nanjing Horticulture* 8:13-14.
24. Yu DC and Wang AL. 1990. Effects of Triacantanol and 6-Benzyladenine on nitrate reductase of *Pinus elliotii* seedlings.  
*Plant Physiology Communications* 6: 34-36.

25. Yu DC. 1989. Effects of abscisic acid to plants under stress. *Science and Technology Communications* 4:32-37.
26. Yu DC. 1987. Studies on the regulators of nitrate reductase in plants. *Science and Technology Communications* 2:36-39.
27. Yu DC. 1986. Effects of plant growth regulators on the fruit ripening. *Thesis*, Zhejiang Forestry University, PRC.

#### GENBANK SUBMISSIONS

1. Yu DC. 1996. Giardavirus genomic sequence. *GenBank Accession No. L13218*.
2. Yu DC, Sakamoto GT and Henderson DR. 1998. Homo sapiens glandular kallikrein enhancer region, complete sequence. *GenBank Accession No. AF113169*.

#### BOOK CHAPTERS

1. Henderson DR, Chen Y and Yu DC. 2001. Attenuated Replication competent adenovirus for prostate cancer: CV706 and CV787. (in press)
2. DC Yu and Henderson DR. 2001. Oncolytic viruses as anti-cancer therapeutics. (in press)

#### JOURNAL HIGHLIGHTS ARTICLES

The paper on Mol. Cell. Biol. 15: 4867-4872 (1995) by DC Yu et al. was selected as a Journal Highlights article entitled "Previously Impenetrable Pathogen Transfected" in *American Society of Microbiology News* 61(11), 591 (1995).

#### ABSTRACTS (SELECTED)

1. Yu DC and Wang J. 1991. Expression of the tobacco mosaic virus coat protein subgenomic RNA in vivo. *The 4th Nationwide Colloquium on Viral Chemistry*. Chengdou, May 17-19.
2. Yu DC and Wang J. 1992. Replication of plant viruses. *The 2nd National Symposium of Young Scientists on Plant Physiology*, Guilin, Oct. 4-8.
3. Yu DC, Wang AL and Wang CC. 1994. Maturation of giardavirus capsid protein involves posttranslational proteolytic processing. *Molecular Parasitology Meeting*, Marine Biology Laboratories, MA, Sept. 17-22.
4. Yu DC, Wang AL and Wang CC. 1994. In vitro expression of giardavirus capsid protein and RDRP protein. *Molecular Parasitology Meeting*, Marine Biology Laboratories, MA, abst.178B.
5. Yu DC, Wang AL and Wang CC. 1995. Virus-mediated expression of firefly luciferase in the parasitic protozoan *Giardia lamblia*. *Molecular Parasitology Meeting*, Marine Biology Laboratories, MA, Sept. 17-22.
6. Yu DC and Wang CC. 1996. Amplification, expression, and packaging of a foreign gene by giardavirus in *Giardia lamblia*. *The First Golden Gate Symposium*, San Francisco, CA, June 1, abst. 72.
7. Yu DC and Wang CC. 1996. Regulatory elements of Giardavirus genome. *Molecular Parasitology Meeting*, Marine Biology Laboratories, MA, Sept. 15-19.
8. Yu DC and Wang CC. 1996. Regulatory elements of giardavirus genome. *The First Golden Gate Symposium*, San Francisco, CA, June 1, abst. 56.
9. Yu DC and Wang CC. 1996. Virus-mediated coexpression of a drug resistance gene and a reporter gene in *Giardia lamblia*. *Molecular Parasitology Meeting*, Marine Biology Laboratories, MA, Sept. 15-19, abst. 255.
10. Yu DC, Wang AL and Wang CC. 1996. Amplification, expression, and packaging of a foreign gene by giardavirus in *Giardia lamblia*. *Molecular Parasitology Meeting*, Marine Biology Laboratories, MA, Sept. 15-19, abst. 355.
11. Yu DC and Henderson DR. 1999. Prostate tumor specific cytolysis and tumor eradication by intravenous administration of CV787, an attenuated replication competent adenovirus containing E3. *Proceedings of the American Association for Cancer Research* 40: 87. 90<sup>th</sup> Annual meeting, AACR, Philadelphia, PA. April 9-14.
12. Ramakrishna NR, Rioseco-Camacho N, Sawyers CL, Yu DC, Henderson DR, Simons JW, and DeWeese TL. 1999. Synergism of ionizing radiation and gene therapy with the replication competent CV706 adenovirus in the LAPC-4 prostate cancer cell line. *Proceedings of the American Association of Cancer Research* 40: 630.
13. Chen Y, Yu DC, and Henderson DR. 1999. Effect of Adenovirus Immunity on the efficacy of oncolytic ARCA in nude mice following intravenous administration *Proceedings of the 1999 AACR.NCA.EORTC Interational Conference (Molecular Targets and Cancer Therapeutics)* 36 #166.
14. Simons JW, Rioseco-Camacho N, Ramakrishna NR, DeWeese TL, Henderson D, Sawyers CL, and Yu DC. 1999. Mechanisms of therapeutic synergy between radiation treatment and adenoviral gene therapy with the replication competent PSA-specific vector CV706 in the LAPC-4

and LNCaP prostate cancer cell lines. *International Journal of Radiation Oncology Biology Physics* 45 (3) (suppl.) 300.

15. Henderson DR, Yu DC, Chen Y and Charlton D. 2000. Pre-existent Adenovirus antibodies inhibits systemic toxicity and antitumor activity of CV706 in the nude mouse LNCaP xenograft model: implications and proposals for human therapy. *Molecular Therapy* 1(5): S269.
16. Chen Y, Yu DC, Charlton D, and Henderson DR. 2000. Pre-existent Ad antibody inhibits systemic toxicity and anti-tumor activity: implications and proposals for human therapy. *Gene Therapy* 65. *Cold Spring Harbor Laboratory*
17. Yu DC, Chen Y, Dilley J, Li Y, Embry M, Zhang H, Nguyen N, Oh J, and Henderson DR. 2000. Antitumor synergy of CV787, a prostate-specific Adenovirus, and paclitaxel and docetaxel. 9<sup>th</sup> *International Conference on Gene Therapy of Cancer* (oral presentation)

#### EDUCATION

- Post-Doctoral Fellow                      Biochemistry and Molecular Virology, 1993-95  
University of California-San Francisco, CA.
- Ph.D.    Molecular Genetics, 1993  
Chinese Academy of Sciences, P.R.China.
- M.Sc.    Plant Physiology, 1989  
Nanjing Forestry University, Nanjing, P.R.China.
- B.Sc.    Agronomy, 1986  
Zhejiang Forestry University, Zhejiang, P.R.China.

#### HONORS AND AWARDS

- *Presidential Award of the Chinese Academy of Sciences* for distinguished dissertation, P.R.China, 1992. (The highest award a student could win in China).
- *Scholarship of Shanghai Institute of Plant Physiology*, Chinese Academy of Sciences, P.R.China, 1991-92. (An honor awarded to the top one student a year).
- *Excellent Student Award*, Zhejiang Forestry University, Zhejiang, P. R. China, in 1983, 1984 and 1985.

#### PROFESSIONAL MEMBERSHIPS

American Association for the Advancement of Science, Chinese Association for Science and Technology, American Association for Cancer Research, American Society for Microbiology and American Society for Gene Therapy



-723 AAGGTGGGGT GATCACAGGA CAGTCAGCCT CGCAGAGACA GAGACCACCC AGGACTGT  
-663 GGGAGAACAT GGACAGGCCC TGAGCCGCAG CTCAGCCAAC AGACACGGAG AGGGAGGG  
-603 CCCCTGGAGC CTTCCCCAAG GACAGCAGAG CCCAGAGTCA CCCACCTCCC TCCACCAC  
-543 TCCTCTCTTT CCAGGACACA CAAGACACCT CCCCCTCCAC ATGCAGGATC TGGGGACT  
-483 TGAGACCTCT GGGCCTGGGT CTCCATCCCT GGGTCAGTGG CGGGGTTGGT GGTACTGG  
-423 ACAGAGGGCT GGTCCCTCCC CAGCCACCAC CCAGTGAGCC TTTTCTAGC CCCAGAG  
-363 ACCTCTGTCA CTTCTGTGTT GGGCATCATC CCACCTTCCC AGAGCCCTGG AGAGCATG  
-303 GAGACCCGGG ACCCTGCTGG GTTCTCTGT CACAAAGGAA AATAATCCCC CTGGTGTG  
-243 AGACCCAAGG ACAGAACACA GCAGAGGTCA GCACTGGGGA AGACAGGTTG TCCTCCCA  
-163 GGATGGGGGT CCATCCACCT TGCCGAARAG ATTTGTCTGA GGAAGTGAAG ATAGAAGG  
-123 AAAAAGAGGA GGGACAAAAG AGGCAGAAAT GAGAGGGGAG GGGACAGAGG ACACCTGA  
-63 AAAGACCACA CCCATGACCC ACGTGATGCT GAGAAGTACT CCTGCCCTAG GAAGAGAC  
-3 AGGGCAGAGG GAGGAAGGAC AGCAGACCAG ACAGTCACAG CAGCCTTGAC AAAACGTT  
57 TGGAACTCAA GCTCTTCTCC ACAGAGGAGG ACAGAGCAGA CAGCAGAGAC CATGGAGT  
117 CCCTCGGCCC CTCCCCACAG ATGGTGATC CCCTGGCAGA GGCTCCTGCT CACAGGTG  
177 GGGAGGACAA CCTGGGAGAG GGTGGGAGGA GGGAGCTGGG GTCTCCTGGG TAGGACAG  
237 CTGTGAGACG GACAGAGGGC TCCTGTTGGA GCCTGAATAG GGAAGAGGAC ATCAGAGA  
297 GACAGGAGTC ACACCAGAAA AATCAAATTG AACTGGAATT GGAAGGGGC AGGAAAAC  
357 CAAGAGTTCT ATTTTCTAG TTAATTGTCA CTGGCCACTA CGTTTTTAAA AATCATAA  
417 ACTGCATCAG ATGACACTTT AAATAAAAC ATAACCAGGG CATGAAACAC TGTCTCA  
477 CGCCTACCGC GGACATTGGA AAATAAGCCC CAGGCTGTGG AGGGCCCTGG GAACCCTC  
537 GAACTCATCC ACAGGAATCT GCAGCCTGTC CCAGGCACTG GGGTGCAACC AAGATC

Figure 2 (11 of 11)